Chemical Ionization of Fluorophenyl *n*-Propyl Ethers: Loss of Propene from the Metastable $[M + D]^+$ Ions

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Chemical ionization (CI) mass spectrometry with the reagents D_2O, CD_3OD, and CD_3CN (given in order of increasing proton affinity) has been used to generate metastable $[M + D]^+$ ions of a series of mono-, di-, and trifluorophenyl *n*-propyl ethers and analogs labeled with two deuterium atoms at the β position of the alkyl group. Loss of propene is the main reaction of the $[M + D]^+$ ions, whereas dissociation with formation of propyl carbenium ions is of minor importance. The combined results reveal that the deuteron added in the CI process can be incorporated in the propene molecules as well as in the propyl carbenium ions. The extent to which the added deuteron is exchanged with the hydrogen atoms of the propyl group is markedly dependent on the position of the fluorine atom(s) on the ring and the exothermicity of the initial deuteron transfer. For 3-fluorophenyl *n*-propyl ether, exchange is not observed if D_2O is the CI reagent, and occurs only to a minor extent in the experiments with the CI reagents CD_3OD and CD_3CN. Similar results are obtained for the 3,5-difluoro- and 2,4,6-trifluorophenyl ethers, whereas significant exchange is observed prior to the dissociations of the $[M + D]^+$ ions of the 4-fluoro- and 2,6-difluorophenyl *n*-propyl ethers, irrespective of the nature of the CI reagent. These results are discussed in terms of the occurrence of initial deuteron transfer either to the oxygen atom or the aromatic ring followed by formation of an ion/neutral complex of a fluorine-substituted molecule and a secondary propyl carbenium ion. Initial deuteron transfer to the oxygen atom is suggested to yield complexes that can react by exchange between the added deuteron and the hydrogen atoms of the original propyl group prior to dissociation. By contrast, initial deuteron transfer to the ring is suggested to lead to complexes that react further by loss of propene molecules containing only the hydrogen/deuterium atoms of the original propyl entity. (J Am Soc Mass Spectrom 1998, 9, 121–129) © 1998 American Society for Mass Spectrometry

The subject of regioselectivity in proton transfer reactions involving polyfunctional organic molecules is of general interest to solution as well as gas-phase conditions. With respect to the gas phase, particular attention has been devoted to proton transfer reactions involving substituted aromatic compounds [1–16]. This interest is related largely to the experimental finding that proton transfer to the substituent is often preferred kinetically, whereas protonation of the aromatic ring can be thermodynamically favored. This applies, for example, to fluorobenzene, which is protonated readily at the halogen atom in the strongly exothermic reaction with CH_5^+ as the Brønsted acid, irrespective of the fact that proton transfer to the ring is significantly more favored from a thermodynamic point of view [10, 13, 15]. A comparable situation is reported for other monosubstituted benzenes, e.g., methyl phenyl ether [13, 17, 18] and aniline [19]. Both of these species are indicated to be protonated kinetically at the heteroatom of the functional group in considerably exothermic reactions, notwithstanding that calculations suggest that the proton affinity of the 4-position of the ring is close to the value for the substituent [19, 20].

Insight into the molecular properties that determine the regioselectivity in proton transfer reactions to substituted aromatic species in the gas phase is also of importance for the application of chemical ionization (CI) mass spectrometry as a method for structure elucidation [1]. In this respect, it is often observed that the initial site of protonation of an organic compound is reflected directly in the dissociations of the generated $[M + H]^+$ ions (see, for example, [21]). A relatively complex situation can arise, however, for polyfunctional organic species that may be protonated at distinct sites and nonetheless dissociate only by a single process. Such a behavior is observed for the metastable $[M + H]^+$ ions of phenyl *n*-propyl ether, which are known to dissociate exclusively by propene loss [22–

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1044-0305/98/$19.00
PII S1044-0305(97)00243-2

Received April 29, 1997
Revised October 6, 1997
Accepted October 9, 1997

25]. As indicated by various studies, CI of phenyl *n*-propyl ether with deuterium labeled reagents leads to metastable $[M + D]^+$ ions that can expel propene molecules containing the deuteron transferred to the ether in the CI process. In a recent paper [25], we suggested that CI of phenyl *n*-propyl ether and methyl-substituted analogs with the reagents D_2O, CD_3OD, and CD_3CN involves competing deuteron transfer to the oxygen atom and the aromatic ring of the ether. Most of the results were discussed on the basis of a simplified statistical model based upon the assumption that, in a strongly exothermic reaction, the deuteron is transferred nonselectively to the oxygen atom or to one of the 2-, 4-, and 6-positions of the ring in phenyl *n*-propyl ether. Moreover, the transfer of a deuteron to the ether function was held responsible for the partial incorporation of the added deuteron in the propene molecules, whereas deuteron transfer to the ring was suggested to yield species that eliminate propene containing only the hydrogen atoms of the original *n*-propyl group. These assumptions, in combination with the statistical analysis, appeared to explain the results obtained for the metastable $[M + D]^+$ ions formed in the reaction of D_3O^+ with the unlabeled phenyl *n*-propyl ether, as well as the species labeled with two deuterium atoms at the β position of the alkyl group. In a more recent study [26], propene loss from the $[M + D]^+$ ions of an extensive series of deuterium labeled phenyl *n*-propyl ethers was examined with D_2O as the CI reagent. The results of this latter study indicate that a relatively simple statistical approach is not capable of explaining the results for propene loss for the metastable $[M + D]^+$ ions of all the differently labeled phenyl *n*-propyl ethers. However, a mechanistic model consistent with all available results was not advanced. In other words, the various models suggest that propene loss from the $[M + D]^+$ ions of phenyl *n*-propyl ether is a complicated process that cannot be fully understood either on the basis of simple statistical models or the assumption that propene loss occurs exclusively from the ions formed by deuteron transfer to the oxygen atom.

With respect to the methyl-substituted ethers, our previous results indicate that propene loss from the metastable $[M + D]^+$ ions of the 4-methylphenyl *n*-propyl ether is induced by competing deuteron transfer to the oxygen atom and the 2- or 6-position of the ring [25]. By contrast, the results for the $[M + D]^+$ ions of the 3-methyl-substituted species appeared to be more consistent with a preference for initial deuteron transfer to the ring, and a similar behavior was suggested for the 3,5-dimethyl, 2,6-dimethyl-, and 2,4,6-trimethylphenyl *n*-propyl ethers. The results for the methyl-substituted ethers indicate that the relative importance of propene loss from ring-protonated species may depend on the presence and position of substituents on the ring. In the present study, this theme is explored further for a series of fluorophenyl *n*-propyl ethers (3-fluoro-, 4-fluoro-, 3,5-difluoro-, 2,6-difluoro-, and 2,4,6-trifluorophenyl *n*-propyl ether) and using the same CI reagents (D_2O, CD_3OD, and CD_3CN) as in our previous work. The fluorine substituted ethers were chosen because the presence of fluorine atoms in the ring were thought to influence the competition between deuteron transfer to the oxygen atom and the ring without participating directly in the overall process.

Experimental

The CI spectra and the mass-analyzed ion kinetic energy (MIKE) [27] spectra were recorded with the use of a Micromass (Manchester, UK) VG ZAB-HFqQ reverse double focusing quadrupole hybrid mass spectrometer [28, 29]. The CI reagent (D_2O, CD_3OD, or CD_3CN) was mixed with one of the fluorine-substituted phenyl *n*-propyl ethers in a volume ratio of 9 to 1. The binary chemical sample was introduced into a combined electron ionization (EI)/CI source through a heated septum inlet (temperature 130°C) until the pressure was in the range of 10^{-4} Pa, as measured by an ionization gauge placed in a side arm to the entrance of the diffusion pump situated beneath the ion source housing. The ion source parameters were: electron energy 70 eV, temperature 150–200°C, ion repeller potential 0 V, and acceleration voltage 8 kV. The relative yields of the various product ions formed in the reactions of the metastable ions were obtained by measuring the relative areas of the metastable peaks. The relative yields of the product ions were reproducible to within 2%.

The fluorine-substituted phenyl *n*-propyl ethers, $F_nC_6H_{5-n}OCH_2CH_2CH_3$ (n = 1–3), were prepared by reacting the appropriate $F_nC_6H_{5-n}O^-$ ion with $CH_3CH_2CH_2Br$ for a period of 24 h in a mixture of water and *N*,*N*-dimethylformamide (DMF) at a temperature of 50°C [30]. The related deuterium labeled compounds with two deuterium atoms at the β position of the *n*-propyl group (>97% D_2) were prepared likewise by a reaction with $CH_3CD_2CH_2Br$. The ethers were purified by preparative gas chromatography (column: reoplex 400, Geigy Company, Ltd., Manchester, UK; temperature 110–150°C). The identity of the compounds was confirmed by ^1H NMR, and the label content was determined by EI mass spectrometry.

Results

The metastable $[M + D]^+$ ions of the fluorophenyl *n*-propyl ethers included in the present study dissociate predominantly by elimination of propene and only to a minor extent with formation of propyl carbenium ions, as indicated in Tables 1 and 2. Loss of HF or DF is not observed for any of the metastable $[M + D]^+$ ions of the present fluorine-substituted species, even though the elimination of HF is a common reaction of protonated fluorobenzenes [15, 31].

For the 3-fluorophenyl *n*-propyl ether, the results given in Table 1 reveal that the metastable $[M + D]^+$ ions exclusively eliminate C_3H_6 if D_3O^+ is the Brønsted acid. By contrast, with $CD_3OD_2^+$ or CD_3CND^+ as the

Table 1. Ratios (in percent) between the losses of (un)labeled propene molecules from the metastable $[M + D]^+$ ions of the 3- and 4-fluorophenyl *n*-propyl ethers and deuterium labeled analogs, together with the relative yields of propyl carbenium ions (see text)[a]

Ether M	CI reagent gas	Carbenium ions				Loss of:			
		$C_3H_7^+$	$C_3H_6D^+$	$C_3H_5D_2^+$	$C_3H_4D_3^+$	C_3H_6	C_3H_5D	$C_3H_4D_2$	$C_3H_3D_3$
3-$FC_6H_4OCH_2CH_2CH_3$	D_2O	≈1				99 (100)			
	CD_3OD	≈1				94 (95)	5 (5)		
	CD_3CN	≈1				94 (95)	5 (5)		
3-$FC_6H_4OCH_2CD_2CH_3$	D_2O			≈1			15 (15)	84 (85)	
	CD_3OD			≈1			14 (14)	81 (82)	4 (4)
	CD_3CN			≈1			14 (14)	81 (82)	4 (4)
4-$FC_6H_4OCH_2CH_2CH_3$	D_2O	≈1	≈1			90 (92)	8 (8)		
	CD_3OD	≈1	≈1			66 (67)	32 (33)		
	CD_3CN	≈1	≈1			51 (52)	47 (48)		
4-$FC_6H_4OCH_2CD_2CH_3$	D_2O			≈1	≈1		19 (20)	73 (74)	6 (6)
	CD_3OD			≈1	≈1		13 (14)	65 (66)	20 (20)
	CD_3CN			≈1	≈1		10 (11)	64 (65)	24 (24)

[a]The normalized ratios for the losses of unlabeled and labeled propene molecules are given in parentheses. These results have been obtained with a neglect of the formation of the propyl carbenium ions.

deuteron donor, loss of C_3H_5D is observed to a minor extent (eqs 1 and 2). For all three CI reagents, $C_3H_7^+$ ions are generated in a low abundance relative to the product ions of propene loss:

$$3\text{-}FC_6H_4OCH_2CH_2CH_3 \xrightarrow{CD_3OD_2^+} [M + D]^+$$

$$[M + D]^+ \xrightarrow{95\%} C_6H_5DFO^+ + C_3H_6 \quad (1)$$

$$[M + D]^+ \xrightarrow{5\%} C_6H_6FO^+ + C_3H_5D \quad (2)$$

The metastable $[M + D]^+$ ions of the 3-fluorophenyl *n*-propyl ether labeled with two deuterium atoms in the propyl group expel only C_3H_5D and $C_3H_4D_2$ with D_2O as the CI reagent. The ratio between these losses is 15:85 if the formation of about 1% of $C_3H_5D_2^+$ ions is neglected. A similar ratio between the loss of C_3H_5D and $C_3H_4D_2$ is observed if CD_3OD or CD_3CN is the CI reagent, notwithstanding that the metastable $[M + D]^+$ ions formed in these systems expel $C_3H_3D_3$ to some extent (Table 1).

A different picture emerges for the 4-fluorophenyl

$$4\text{-}FC_6H_4OCH_2CH_2CH_3 \xrightarrow{CD_3OD_2^+} [M + D]^+$$

$$[M + D]^+ \xrightarrow{67\%} C_6H_5DFO^+ + C_3H_6 \quad (3)$$

$$[M + D]^+ \xrightarrow{33\%} C_6H_6FO^+ + C_3H_5D \quad (4)$$

n-propyl ether. For the unlabeled species, the metastable $[M + D]^+$ ions formed with D_2O as the CI reagent eliminate C_3H_6 and C_3H_5D in a ratio of 92:8 and, in addition, dissociate to yield $C_3H_7^+$ and $C_3H_6D^+$ ions (Table 1). Furthermore, the metastable $[M + D]^+$ ions expel C_3H_6 and C_3H_5D in a ratio of 67:33 with CD_3OD as the CI reagent (eqs 3 and 4). With CD_3CN, the ratio changes even more in favor of loss of C_3H_5D; that is, C_3H_6 and C_3H_5D are expelled in a ratio of 52:48 from the $[M + D]^+$ ions generated in this particular system (Table 1).

The results for the 4-fluorophenyl *n*-propyl ether labeled with two deuterium atoms at the β position also reveal the marked tendency of the metastable $[M + D]^+$ ions to expel propene molecules that contain the deuterium atom from the CI reagent. This is particularly apparent in the experiments with CD_3OD or CD_3CN as the CI reagent. In these systems, the ratio between the losses of C_3H_5D, $C_3H_4D_2$, and $C_3H_3D_3$ is 14:66:20 and 11:65:24, respectively (see Table 1).

The metastable $[M + D]^+$ ions of the unlabeled 3,5-difluorophenyl *n*-propyl ether behave somewhat similarly to the related ions of the 3-fluorophenyl *n*-propyl ether in the sense that only C_3H_6 is expelled and minor amounts of $C_3H_7^+$ ions are formed (Table 2). No variation in the results for the 3,5-difluorophenyl *n*-propyl ether is observed if the CI reagent is changed from D_2O to either CD_3OD or CD_3CN. Similarly, the metastable $[M + D]^+$ ions of the labeled ether eliminate C_3H_5D and $C_3H_4D_2$ in a ratio of 10 to 90, irrespective of the nature of the CI reagent.

A distinct behavior is observed also for the metastable $[M + D]^+$ ions of the 2,6-difluorophenyl *n*-propyl ether, as revealed by the results in Table 2. The $[M + D]^+$ ions of this ether dissociate on the microsecond timescale to yield 15%–20% propyl carbenium ions in addition to the product ions of propene expulsion. For the $[M + D]^+$ ions of the unlabeled 2,6-difluorine substituted ether, the ratio between the $C_3H_7^+$ and

Table 2. Ratios (in percent) between the losses of (un)labeled propene molecules from the metastable $[M + D]^+$ ions of the 2,6- and 3,5-difluorophenyl *n*-propyl ethers as well as the 2,4,6-trifluorophenyl *n*-propyl ether and deuterium labeled analogs, together with the relative yields of propyl carbenium ions (see also text)

Ether M	CI reagent gas	Carbenium ions[a]				Loss of:[b]			
		$C_3H_7^+$	$C_3H_6D^+$	$C_3H_5D_2^+$	$C_3H_4D_3^+$	C_3H_6	C_3H_5D	$C_3H_4D_2$	$C_3H_3D_3$
3,5-$F_2C_6H_3OCH_2CH_2CH_3$	D_2O	≈1				99			
	CD_3OD	≈1				99			
	CD_3CN	≈1				99			
3,5-$F_2C_6H_3OCH_2CD_2CH_3$	D_2O			≈1			10 (10)	89 (90)	
	CD_3OD			≈1			10 (10)	89 (90)	
	CD_3CN			≈1			10 (10)	89 (90)	
2,6-$F_2C_6H_3OCH_2CH_2CH_3$	D_2O	15 (88)	2 (12)			76 (92)	7 (8)		
	CD_3OD	17 (85)	3 (15)			70 (88)	10 (12)		
	CD_3CN	14 (78)	4 (22)			70 (85)	12 (15)		
2,6-$F_2C_6H_3OCH_2CD_2CH_3$	D_2O			16 (89)	2 (11)		7 (9)	69 (84)	6 (7)
	CD_3OD			18 (86)	3 (14)		5 (6)	66 (84)	8 (10)
	CD_3CN			15 (83)	3 (17)		6 (7)	66 (81)	10 (12)
2,4,6-$F_3C_6H_2OCH_2CH_2CH_3$	D_2O	≈1				99			
	CD_3OD	8				92			
2,4,6-$F_3C_6H_2OCH_2CD_2CH_3$	D_2O			2			18 (18)	78 (80)	2 (2)
	CD_3OD			10 (91)	1 (9)		10 (11)	75 (85)	4 (4)

[a]The normalized abundance ratios of carbenium ions are given in parentheses (obtained with a neglect of the losses of unlabeled and labeled propene molecules).
[b]The normalized ratios for the losses of unlabeled and labeled propene molecules are given in parentheses (obtained by disregarding the formation of propyl carbenium ions).

$C_3H_6D^+$ ions is 88:12 if D_2O is the CI reagent, as indicated in eqs 5 and 6. This ratio changes somewhat in favor of formation of the $C_3H_6D^+$ ion if CD_3OD or CD_3CN is the CI reagent; that is, the metastable $[M + D]^+$ ions formed in reaction with $CD_3OD_2^+$ dissociate to yield $C_3H_7^+$ and $C_3H_6D^+$ ions in an abundance ratio of 85:15, and with CD_3CND^+ as the deuteron donor, a ratio of 78:22 is obtained (Table 2).

A similar picture is obtained for the competing losses of C_3H_6 and C_3H_5D from the metastable $[M + D]^+$ ions of the unlabeled 2,6-difluorine-substituted ether. For example, the ratio between the losses of C_3H_6 and C_3H_5D is 92:8 with D_2O as the CI reagent, whereas this ratio is 85:15 if CD_3CN is used (Table 2).

The observations for the unlabeled 2,6-difluorophenyl *n*-propyl ether are further corroborated by the results for the deuterium labeled species. In particular, the metastable $[M + D]^+$ ions of this ether dissociate to yield $C_3H_5D_2^+$ and $C_3H_4D_3^+$ ions in a ratio that varies in favor of the latter ions as the CI reagent is changed from D_2O to CD_3OD or CD_3CN (Table 2). Likewise, these $[M + D]^+$ ions dissociate by expelling C_3H_5D, $C_3H_4D_2$, and $C_3H_3D_3$ in a ratio that changes somewhat as the CI reagent is altered. In terms of relative importance, this variation is manifested most clearly in the relative extent of the loss of $C_3H_3D_3$. For example, the normalized extent of $C_3H_3D_3$ loss is 7% with D_2O as the reagent, whereas the relative importance of the loss of this labeled propene becomes 12% if CD_3CN is used.

$$2,6\text{-}F_2C_6H_3OCH_2CH_2CH_3 \xrightarrow{D_3O^+} [M + D]^+ \begin{cases} \xrightarrow{88\%} C_3H_7^+ + C_6H_3DF_2O & (5) \\ \xrightarrow{12\%} C_3H_6D^+ + C_6H_4F_2O & (6) \end{cases}$$

The metastable $[M + D]^+$ ions of the unlabeled 2,4,6-trifluorophenyl *n*-propyl ether also dissociate to yield $C_3H_7^+$ ions. With D_2O as the CI reagent, only minor amounts of the $C_3H_7^+$ ions are formed, whereas the relative yield of these product ions is 8% in the experiments with CD_3OD (Table 2). Only C_3H_6 is expelled from the $[M + D]^+$ ions of the unlabeled ether, whereas $C_3H_3D_3$ is eliminated to a minor extent for the metastable $[M + D]^+$ ions of the 2,4,6-$F_3C_6H_2OCH_2CD_2CH_3$ ether formed either in reaction with D_3O^+ or $CD_3OD_2^+$.

In the experiments with the unlabeled di- and trifluorophenyl *n*-propyl ethers and CD_3CN as the CI reagent, the selected metastable ions are observed to undergo the additional loss of a neutral fragment with a mass of 44 Da. In principle, this neutral fragment could correspond to C_3H_8; that is, the original propyl group of the parent compound and a hydrogen atom from the aromatic ring could be expelled from the metastable ions either as one neutral species or as C_3H_6 and H_2. However, in the experiments with the deuterium labeled di- and trifluorophenyl ethers, no loss of a neutral fragment with an elemental composition of $C_3H_6D_2$ is observed. A more likely explanation for these observations could be that in the experiments with unlabeled ethers, part of the collision complexes formed in the reaction with CD_3CND^+ may expel C_3H_8 or C_3H_6

+ H_2 in the ion source. As exemplified in eq 7, such a process results in ions with a nominal mass-to-charge ratio of 174 for the 2,6-difluorophenyl *n*-propyl ether. In other words, this reaction leads to ions that are isobaric with the $[M + D]^+$ ions of the 2,6-difluorophenyl *n*-propyl ether (*m*/*z* 174), and a similar situation applies to the 2,4,6-trifluorophenyl *n*-propyl ether.

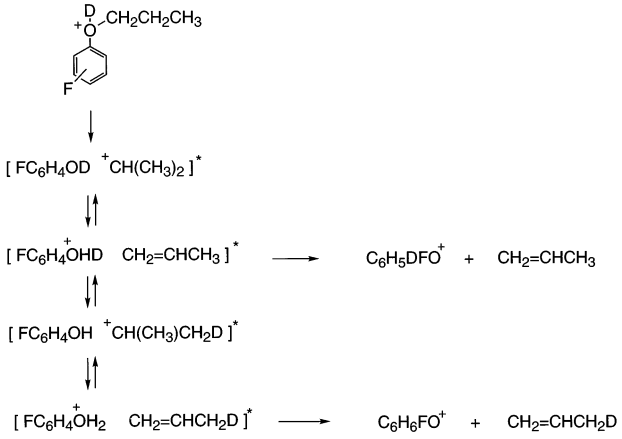
$$2,6\text{-}F_2C_6H_3OCH_2CH_2CH_3 \xrightarrow[-C_3H_8]{CD_3CND^+} C_8H_2D_4F_2NO^+ \longrightarrow C_6H_2DF_2O^+ + C_2D_3N \quad (7)$$

m/*z* 174

In the experiments with the unlabeled difluorophenyl *n*-propyl ethers and CD_3CN as the CI reagent, the loss of a neutral fragment with a mass of 44 Da accounts for 10%–15% of the total yield of the product ions formed in the dissociation of the metastable and isobaric ions selected according to a nominal mass-to-charge ratio value of 174. In the experiments with the 2,4,6-trifluorophenyl *n*-propyl ether, the main peak in the MIKE spectra corresponds to the loss of a neutral fragment with a mass of 44 Da. Owing to the possible predominance of the formation of ions that are isobaric with the $[M + D]^+$ ions of the trifluorine-substituted species, the experiments with this ether were limited to the CI reagents D_2O and CD_3OD.

Discussion

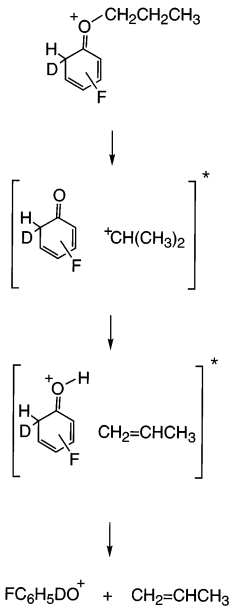
The combined results for the fluorine-substituted phenyl *n*-propyl ethers reveal that interchange can occur between the deuteron transferred in the CI process and the hydrogen atoms of the propyl group prior to the loss of propene or the formation of propyl carbenium ions. The results also indicate that the occurrence of this interchange depends on the nature of the CI reagent. In this respect it should be mentioned that the proton affinities of the unlabeled analogs are reported to be 697 kJ mol^{-1} (H_2O), 761 kJ mol^{-1} (CH_3OH), and 788 kJ mol^{-1} (CH_3CN) [32]. These values indicate that initial deuteron transfer to the given fluorine-substituted ethers becomes less exothermic by 64 kJ mol^{-1} if water is replaced for methanol and by 27 kJ mol^{-1} if acetonitrile is used instead of methanol. In addition, the combined results reveal a strong dependence of the interchange on the position of the fluorine atom(s) on the aromatic ring of the ether. This dependence indicates that the initial deuteron transfer to the ether is influenced by the presence of the fluorine atom(s) on the ring either thermodynamically and/or kinetically. Unfortunately, no proton affinities are available for the present fluorine-substituted ethers and no studies have been concerned with the kinetic aspects of proton transfer to these types of compounds. Obviously, the lack of insight into deuteron transfer to the fluorine-substituted ethers limits the discussion of the mechanistic aspects of the dissociation of the metastable $[M + D]^+$ ions to more qualitative considerations based on the trends in the product ion distributions as the CI reagent is changed.



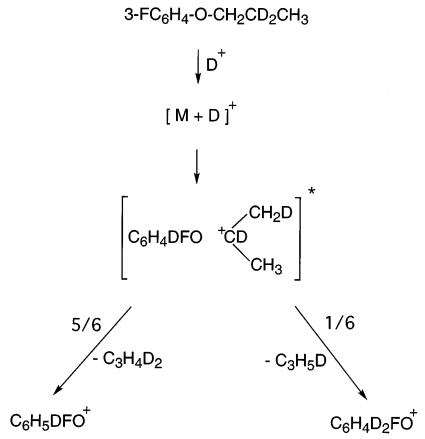
Scheme I. Proposed mechanism for the loss of propene as initiated by deuteron transfer to the oxygen atom of the unlabeled monosubstituted fluorophenyl *n*-propyl ethers (see also text).

In our previous study concerned with the loss of propene from the metastable $[M + D]^+$ ions of phenyl *n*-propyl ether and a series of methyl-substituted analogs, a mechanistic picture was advanced that involved competing deuteron transfer to the oxygen atom and the aromatic ring [25]. A similar situation may apply to the fluorine-substituted ethers in that none of the present results indicate that initial deuteron transfer to a fluorine atom plays a role in the dissociations of the metastable $[M + D]^+$ ions formed with the selected CI reagents (see Results). The mechanistic picture for the loss of propene from the ions formed by deuteron transfer to the oxygen atom or the ring is shown in Schemes I and II for the monofluorine substituted ethers.

For the ions formed by initial deuteron transfer to the oxygen atom, the reaction is formulated in Scheme I as proceeded by a cleavage of the bond between the oxygen atom and the α-carbon atom of the propyl group occurring concomitant with a 1,2-hydride shift in the incipient primary propyl carbenium ion [33]. This results in an ion-neutral complex [34–36] composed of a fluorophenol molecule and a secondary propyl carbenium ion that reacts subsequently by proton transfer prior to the loss of propene. The ions formed by deuteron transfer to the aromatic ring (Scheme II) react with formation of an ion-neutral complex of a fluorine-substituted cyclohexadienone and a secondary propyl carbenium ion prior to the occurrence of proton transfer and propene expulsion. In these hypothetical schemes, it is assumed explicitly that the incorporation of the added deuteron in the propene molecules is a result of initial transfer to the oxygen atom, whereas initial transfer to the ring is considered to lead to ions that



Scheme II. Proposed mechanism for the loss of propene as initiated by deuteron transfer to the aromatic ring of the unlabeled monosubstituted fluorophenyl *n*-propyl ethers (see also text). For reasons of simplicity, propene loss is shown only for the species formed by deuteron transfer to the 2- or 6-position.



Scheme III. Reaction sequence for the loss of propene as initiated by deuteron transfer to the labeled 3-fluorophenyl *n*-propyl ether. The numbers given for the reactions of the intermediate ion-neutral complexes represent statistical probabilities for the transfer of a proton and deuteron, respectively, from the methyl groups of the carbenium ion, as estimated ignoring an isotope effect.

expel propene molecules containing only the hydrogen atoms of the original propyl group in the parent compound (vide infra).

Based on the mechanistic pictures shown in Schemes I and II, it could be proposed that the exclusive occurrence of C_3H_6 loss from the metastable $[M + D]^+$ ions formed in the reaction of D_3O^+ with the 3-fluorine-substituted ether (Table 1) reflects that the deuteron is transferred preferentially or exclusively to the ring. In the reactions with $CD_3OD_2^+$ or CD_3CND^+, deuteron transfer to the oxygen atom of the ether could then be thought to become relatively more important and result in the occurrence of C_3H_5D loss (Table 1). However, the absence of exchange with the propyl hydrogen atoms in the dissociation of the $[M + D]^+$ ions formed with D_3O^+ as the deuteron donor could also be related to the internal energy distribution of the metastable ions. As mentioned, deuteron transfer from D_3O^+ to the ether is significantly more exothermic than, for example, from the $CD_3OD_2^+$ ion. As a result, the average internal energy of the metastable $[M + D]^+$ ions could be thought to be higher if these ions are generated by deuteron transfer from D_3O^+ instead of from the $CD_3OD_2^+$ ion. This implies that deuteron transfer from D_3O^+ to the oxygen atom may lead to $[C_6H_5OD\ ^+CH(CH_3)_2]$ complexes with a relatively high internal energy. Thus, the ensuing proton transfer may be essentially irreversible and lead directly to dissociation without the occurrence of hydrogen-deuterium exchange (see also Scheme I). With respect to the minor loss of C_3H_5D from the metastable ions formed in the reaction with $CD_3OD_2^+$ or CD_3CND^+, the occurrence of this reaction could be taken to mean that the exchange competes with dissociation only at relatively low internal energies of the metastable ions.

These considerations are supported by the results for the deuterium labeled 3-fluorophenyl *n*-propyl ether. Significantly, the observed ratio between the losses of C_3H_5D and $C_3H_4D_2$ in the experiments with D_2O (15:85) is close to the ratio of 16.7:83.3, as calculated on the basis of a pathway involving formation of a $[C_6FH_4DO\ ^+CD(CH_3)CH_2D)]$ complex that reacts further by irreversible transfer of a proton or deuteron from the methyl groups prior to dissociation (neglecting isotope effects; see Scheme III). With the reagents CD_3OD and CD_3CN, the minor extent of $C_3H_3D_3$ loss may also indicate here that deuteron transfer to the ring is less important than with D_2O as the reagent and/or that deuteron transfer to the oxygen atom leads to ion/neutral complexes with a relatively low internal energy. Irrespective of the occurrence of $C_3H_3D_3$ loss, the ratio between the losses of C_3H_5D and $C_3H_4D_2$ (15:85; see also Table 1) is still close to that predicted based on the predominant occurrence of the process shown in Scheme III.

For the 4-fluorophenyl *n*-propyl ether the results reveal that the extent of exchange between the deuteron transferred in the CI process and the propyl hydrogen atoms depends strongly upon the nature of the reagent. If the $[M + D]^+$ ions are formed in the significantly exothermic reaction with D_3O^+, the tendency to expel C_3H_5D is relatively low (Table 1). This could reflect that the deuteron transfer to the ring of the 4-fluorine substituted ether is preferred, and/or that the $[M + D]^+$ ions formed by deuteron transfer to the oxygen atom dissociate to a significant extent without undergoing the exchange indicated Scheme I. The relative extent of the loss of C_3H_5D increases significantly, however, as

the initial deuteron transfer to the 4-fluorophenyl *n*-propyl ether becomes less exothermic (Table 1). In the limiting case of exclusive occurrence of deuteron transfer to the oxygen atom and exchange of one deuterium atom with six hydrogen atoms (see also Scheme I), the ratio between the losses of C_3H_6 and C_3H_5D is estimated to be 28.6:71.4. Notwithstanding that the ratios obtained experimentally for CD_3OD (67:33) or CD_3CN (52:48) are still far from this estimated ratio, the results may indicate a preference for deuteron transfer to the oxygen atom followed by propene loss.

These suggestions are in line with the results for the metastable $[M + D]^+$ ions of the 4-fluorophenyl *n*-propyl ether labeled with two deuterium atoms at the β position of the alkyl group. For this species, the ratio between the losses of C_3H_5D, $C_3H_4D_2$, and $C_3H_3D_3$ from the $[M + D]^+$ ions formed in the less exothermic reactions may also be taken to reflect an increased importance of initial deuteron transfer to the oxygen atom, followed by formation of a ion-molecule complex composed of a $4\text{-}FC_6H_4OD$ molecule and a $(CDH_2)(CH_3)CD^+$ ion. In the extreme case of the exclusive occurrence of this process, in combination with the assumption that hydride or deuteride shifts are not occurring in the secondary propyl carbenium ion, exchanges between two deuterium atoms and the five hydrogen atoms of the ionic part of the $[4\text{-}FC_6H_4OD(CDH_2)(CH_3)CD^+]$ complex are predicted to lead to a ratio of 4.8:47.6:47.6 between the losses of C_3H_5D, $C_3H_4D_2$, and $C_3H_3D_3$. As mentioned for the related ion of the unlabeled ether, the experimental findings are far from such a limiting situation. In other words, these considerations may imply either that propene loss is occurring also from the ring-deuteronated species and/or that the exchange in the intermediate complexes formed as a consequence of initial deuteron transfer to the oxygen atom is only partially complete.

The metastable $[M + D]^+$ ions of the unlabeled 3,5-difluorophenyl *n*-propyl ether expel C_3H_6 only, irrespective of the exothermicity of the initial deuteron transfer. Moreover, no loss of $C_3H_3D_3$ is observed for the related ions of the labeled ether, and no variation in the ratio between the losses of C_3H_5D and $C_3H_4D_2$ is observed as the CI reagent is varied. Although the internal energy of the intermediate complexes generated by deuteron transfer to the oxygen atom may be such that incorporation of the added deuteron in the propene molecules is not occurring (vide supra), the results are not in disagreement with a predominant occurrence of deuteron transfer to the ring followed by propene loss. For the $[M + D]^+$ ions of the positional isomer, 2,6-difluorophenyl *n*-propyl ether, an even less clear picture emerges. For this particular system, relatively abundant carbenium ions are generated. For the ions formed from the unlabeled ether, the increase in the relative yield of the $C_3H_6D^+$ ion as the CI reagent is changed from D_2O to CD_3OD or CD_3CN reveals directly the more pronounced tendency to undergo hydrogen-deuterium exchange prior to dissociation as the initial deuteron transfer becomes less exothermic. This is also indicated—as expected—by the ratios for the competing losses of C_3H_6 and C_3H_5D as given in Table 2.

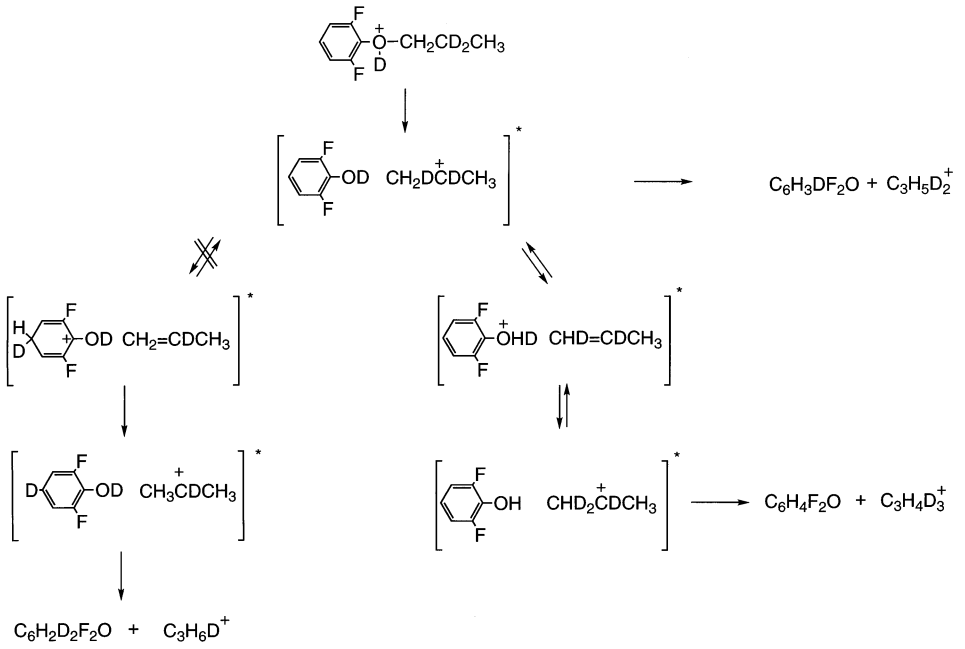
For the labeled 2,6-difluorophenyl *n*-propyl ether, the formation of the $C_3H_5D_2^+$ and $C_3H_4D_3^+$ ions may be visualized as indicated in Scheme IV. The initial step in the reaction sequence is deuteron transfer to the oxygen atom, which is indicated to be succeeded by cleavage of the ether bond accompanied by a 1,2-deuteride shift in the evolving carbenium ion. The complex thus formed may then dissociate to yield the $C_3H_5D_2^+$ ions or undergo a proton transfer with formation of a second ion/neutral complex as shown in Scheme IV. Deuteron transfer back to the propene molecule may then lead to dissociation with formation of the $C_3H_4D_3^+$ ions.

The most significant observation for this system is that no $C_3H_6D^+$ ions are formed in the dissociation of the metastable $[M + D]^+$ ions of the labeled 2,6-difluorophenyl *n*-propyl ether. If such ions were to be formed, this would require the occurrence of deuteron transfer to the ring of the fluorine-substituted phenol molecule in the first ion-molecule complex shown in Scheme IV, followed by back donation of a proton to the propene molecule, and then dissociation. Thus, the absence of $C_3H_6D^+$ ions indicates that interchange between the deuterium atoms of the propyl group and the hydrogen atoms of the aromatic ring is unlikely to play a role in the dissociation of the metastable $[M + D]^+$ ions of this ether. Moreover, the absence of the formation of $C_3H_6D^+$ ions irrespective of the nature of the CI reagent (Table 2) supports the view that the exchange between the added deuteron and hydrogen/deuterium atoms of the propyl entity involves initial deuteron transfer to the oxygen atom of the ether.

The results for the metastable $[M + D]^+$ ions of the 2,4,6-trifluorophenyl *n*-propyl ether appear to some extent to be intermediate with respect to the findings for the two difluorine-substituted species. For the ions of the unlabeled ether, the absence of incorporation of the added deuteron either in the propyl carbenium ions or the propene molecules could be in line with predominant deuteron transfer to the aromatic ring. For the labeled species, the metastable $[M + D]^+$ ions are observed to expel some $C_3H_3D_3$ molecules and also form $C_3H_4D_3^+$ ions in a low relative yield if CD_3OD is the CI reagent. Deuteron transfer to the oxygen atom may thus occur and can lead to some exchange with hydrogen atoms of the propyl group, regardless of the fact that the combined findings for the unlabeled and labeled ether indicate that this process is sensitive to the presence of deuterium atoms in the propyl group.

Conclusions

The present series of results reveals that the metastable $[M + D]^+$ ions of the fluorine-substituted phenyl *n*-propyl ethers all display a distinct behavior with respect to the incorporation of the deuteron added in the



Scheme IV. Possible mechanism for the formation of the $C_3H_5D_2^+$ and $C_3H_4D_3^+$ carbenium ions in the reactions of the metastable $[M + D]^+$ ions formed by deuteron transfer to the oxygen atom of the labeled 2,6-difluorophenyl *n*-propyl ether. The formation of $C_3H_6D^+$ ions by a pathway involving deuteron transfer to the 4-position of the ring of the fluorine-substituted molecule in the first formed ion/neutral complex is hypothetical (see also text).

CI process into the expelled propene molecules and the propyl carbenium ions generated as free ions. Most of the results can be taken to mean that dissociation occurs from $[M + D]^+$ ions formed by competing deuteron transfer to the oxygen atom and the aromatic ring. For the 3-fluoro-, 3,5-difluoro-, and 2,4,6-trifluorophenyl *n*-propyl ethers the results are indicative of a significant contribution to the overall loss of propene from ions generated by deuteron transfer to the aromatic ring, irrespective of whether D_2O, CD_3OD, or CD_3CN is the CI reagent. For the 4-fluorophenyl *n*-propyl ether and the latter two reagents, the extensive incorporation of the added deuteron in the propene molecules is taken to mean that deuteron transfer to the oxygen atom becomes more important as the initial step in the CI process becomes less exothermic. A somewhat similar situation applies to the 2,6-difluorophenyl *n*-propyl ether, even though the metastable $[M + D]^+$ ions of this species dissociate to yield significant amounts of propyl carbenium ions. Notably, no $C_3H_6D^+$ ions are generated in the reactions of the $[M + D]^+$ ions of the 2,6-difluorophenyl *n*-propyl ether labeled with two deuterium atoms at the β position of the alkyl group. This finding is suggested to support the proposal that deuteron transfer to the oxygen atom can lead to the exchange with the hydrogen atoms of the propyl group, whereas initial deuteron transfer to the ring may lead to ions that expel propene molecules containing only hydrogen atoms from the *n*-propyl group of the parent ether.

Acknowledgments

The authors thank the Netherlands Organization for Scientific Research (SON/NWO) for financial support and Mrs. T. A. Molenaar-Langeveld for her assistance during the synthesis of some of the deuterium labeled ethers.

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